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VIA FEDERAL EXPRESS

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Dockets Management Branch
Food and Drug Administration
Room 1061, HFA-305
5630 Fishers Lane
Rockville, MD 20852

**Re: Comments on Use of Ozone-Depleting Substances
Docket No. 97N-0023**

Dear Sir or Madam:

Please file the attached letter in Docket No. 97N-0023 on the Use of Ozone-Depleting Substances. The letter describes the position of the National Pharmaceutical Alliance and the Generic Pharmaceutical Industry Association with respect to Protocol Decision XI/15 of the Montreal Protocol on Substances that Deplete the Ozone Layer. We are submitting three (3) copies.

Respectfully submitted,



Gary L. Yingling

GLY/rld
Enclosure(s)

97N-0023

09621

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December 6, 1999

VIA FACSIMILE

Mr. Christopher C. Jennings
Deputy Assistant to the President
for Health Policy Development
The White House
1600 Pennsylvania Avenue
Washington, DC 20502

**Re: Opposition of Generic Pharmaceutical Industry
to Montreal Protocol - Decision XI/15**

Dear Mr. Jennings:

The Generic Pharmaceutical Industry Association ("GPIA") and the National Pharmaceutical Alliance ("NPA") – trade associations comprised of manufacturers and distributors of safe, effective and affordable pharmaceuticals, and providers of technical services and goods to these firms – write this letter to inform you of a grave risk to the public health and to request your assistance in addressing this risk. We are referring to a Protocol Decision ("Decision XI/15") proposed by the Costa Rican delegation to the Montreal Protocol on Substances that Deplete the Ozone Layer ("Montreal Protocol") during the 19th meeting of the Open-Ended Working Group of the Parties. It is our understanding that Decision XI/15 was considered by the participants of the 11th meeting of the Parties, scheduled for November 29 – December 3, 1999, in Beijing, China.

Decision XI/15, which purports to facilitate the worldwide transition to a chlorofluorocarbon-free environment, would greatly hinder the availability of generic pharmaceutical products packaged in metered dose inhalers ("MDI") that contain chlorofluorocarbons ("CFC"), by setting an arbitrary deadline after which new drugs utilizing CFC MDIs cannot enter the U.S. market. According to the U.S. Food and Drug Administration ("FDA"), these CFC-containing MDIs are the most widely accepted delivery system for administering drugs by oral inhalation for the treatment of asthma and chronic obstructive pulmonary disease ("COPD").¹ These

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medical conditions affect over 20 million children and adults in the United States.² In essence, the proposal would erect an impenetrable wall against the market entry of CFC-containing drugs, providing an unearned and potentially unending monopoly for those MDI manufacturers who had obtained FDA approval of their drug applications prior to November 29, 1999. The proposal erects this wall by requiring the U.S., as a party to the Montreal Protocol, to prohibit the marketing of any "new" CFC-containing MDI drug products after that date. To the extent that the Decision's prohibition against "new drugs" includes generic equivalents to previously-approved drug products, GPIA and NPA are opposed to Decision XI/15.

Background. The production of ozone-depleting substances is being phased out worldwide under the terms of the Montreal Protocol.³ In accordance with this treaty, and under authority of Title VI of the Clean Air Act,⁴ the manufacture of CFCs in the U.S. was generally banned as of January 1, 1996.⁵ Since that time, however, essential use exemptions have been routinely granted in the U.S. for the production of CFCs for MDIs used in treating asthma and COPD. According to FDA, this medical need is supported by the United Nations Environment Program ("UNEP") Technical and Economic Assessment Panel ("TEAP"). The medical need is so great that the essential use exemption for MDI drugs represents the only commercial purpose for which CFCs can be produced in the U.S.⁶

Through Decision XI/15, however, the medical need for CFC-containing MDI drugs would be thwarted by setting an arbitrary deadline after which new products of this type, including generic drugs, cannot enter the U.S. market. For example, Decision XI/15 recommends that the Parties determine "essentiality", which governs the essential use exemption that permits the continued marketing of MDI drugs, according to the following criteria: (1) the MDI product has been approved by the national health authority prior to the Eleventh Meeting of the Parties to the Montreal Protocol (November 29, 1999), unless that authority has determined that the product will serve an otherwise unmet medical need; (2) the MDI product is not intended for export to a Party that has determined the product to be non-essential; (3) the company requesting CFCs is actively pursuing research and development for CFC-free alternatives for its products; (4) the company does not increase its strategic reserves of CFCs beyond reasonable levels; (5) the company decreases its strategic reserves of CFCs in line with the declining annual demand; and (6) the company commits to destroying any of its remaining strategic reserves of CFCs upon completion of its MDI transition. The implementation of these unreasonable criteria would jeopardize the health of American consumers and prohibit the marketing of cost-effective generic drugs.

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Issues of Concern. GPIA and NPA understand that, by prohibiting “new drugs”, Decision XI/15 may be interpreted to prohibit FDA approval of generic drugs that are equivalent to previously-approved (i.e., “old”) brand-name MDI drugs, in addition to prohibiting FDA approval of new brand-name drugs. As such, GPIA and NPA oppose Decision XI/15 for the five reasons explained below. We need your help to combat this overreaching international law and to protect American consumers.

First, Decision XI/15 endangers the health of millions of Americans who suffer from respiratory conditions by limiting patient access to affordable medications. Current medical and scientific knowledge supports the view that many MDI drugs formulated with CFCs are essential use products. Although the Decision would likely prohibit the marketing of generic drugs, currently-marketed brand-name MDI drugs would continue to be marketed. Yet, the essential use of the product, whether brand-name or generic equivalent, would remain the same. Thus, CFC-containing MDI drugs should not be internationally regulated in a way that would result in the continued marketing of brand-name, essential-use drugs but not essential-use generic equivalents.

Second, Decision XI/15 is contrary to FDA’s science-based decision on the appropriate U.S. transition away from CFC-containing MDI drugs. FDA’s primary objective is to ensure that the millions of asthma and COPD patients in the U.S. continue to have access to an adequate number of safe and effective treatment options for these life-threatening conditions.⁷ There is no question that the U.S. Government should meet its obligation under the Montreal Protocol by implementing its own unique transition strategy to a CFC-free environment. Nevertheless, competing public health concerns also exist and have been carefully balanced by FDA and EPA. In so doing, FDA’s Medical Policy Coordinating Committee worked strenuously to evaluate all the scientific, technical, regulatory and clinical issues affected by the transition to CFC-free drug products and to develop a transition strategy that would account for all of the U.S. stakeholders who have competing concerns in the area.⁸

In keeping with its balanced transition strategy, FDA has greatly limited the numbers of pharmaceuticals that may contain CFCs, by declaring that all such products are “new drugs” that cannot be lawfully marketed in the U.S. unless they are FDA-approved through the new (or abbreviated) drug application process or fall within one of the few exceptions permitted for drugs. 21 C.F.R. § 2.125 (1999).⁹ Moreover, FDA provides a scientifically rigorous mechanism with which drug manufacturers must comply before obtaining an exception to market their products

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(i.e., "essential use" status). Specifically, drug manufacturers must provide FDA with data showing that: (1) there are no technically feasible alternatives to the use of CFCs in the product; (2) the product provides a substantial health benefit that would not be obtained without the CFC; and (3) the use does not involve a significant nor unwarranted release of CFCs into the atmosphere. 21 C.F.R. § 2.125 (1999).¹⁰ FDA's approach is reasonable, scientifically-based, and addresses the competing regulatory concerns, including the market entry of equivalent and affordable generic drugs. FDA's approach should not be supplanted by Directive XI/15.

Third, Decision XI/15 is contrary to law because it provides an unwarranted monopoly within the pharmaceutical industry, which is directly opposed to the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act.¹¹ That law represents Congress' efforts to delicately balance the competing objectives of encouraging pharmaceutical innovation while providing American consumers with affordable generic drugs. In contrast to these balanced objectives, Decision XI/15 will result in an artificially preserved marketplace for CFC-containing MDI drugs with little competition. Such monopoly periods almost always lead to inflated prices. Thus, Decision XI/15 will wield a double-blow to patients by limiting their medical treatment choices while also likely forcing them to pay exorbitant prices for the few choices they have remaining.

Decision XI/15 also defies the Hatch-Waxman Act by requiring research and development into CFC-free technology. Such testing is prohibited for generic manufacturers, who cannot include that type of clinical test within the drug application required by FDA for a generic drug.¹²

Fourth, Decision XI/15 is contrary to public policy. Implementation of the Decision will adversely affect members of the generic drug industry who have worked for years with FDA's Office of Generic Drugs to develop safe and effective generic alternatives to brand-name MDI products based on currently available propellant technologies. And the development of CFC-free technologies is no solution, since generic manufacturers will be locked out of the market for new FDA-approved drugs for at least 20 years under current U.S. patent law. Moreover, the

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Decision would interfere with the practice of medicine by unreasonably limiting the MDI choices available to the physician. The Decision also would interfere with the patient's right to receive a cost-effective drug that the patient considers the most beneficial for his or her medical condition.

Fifth, the recommendations made by Decision XI/15 are unwieldy and unnecessary given the progress of FDA and the pharmaceutical industry in this area. In its preamble, Decision XI/15 acknowledges that the transition to CFC-free technology will have progressed satisfactorily by the year 2000. Furthermore, the use of CFC propellants by the pharmaceutical industry is minimal when compared to the use of CFC propellants in products sold by other industries. For example, the total worldwide use of CFC propellants for pharmaceutical MDI products is less than 0.5% of the total worldwide use of CFCs for all purposes. Moreover, GPIA and NPA believe that the use of CFC propellants in pharmaceuticals has a minimal impact on the environment. It is our understanding that pharmaceutical MDI products contribute less than 1% of the total CFC emissions into the atmosphere. Given the minimal number of CFC-containing pharmaceutical products and their overall diminutive effect on the environment, the Costa Rica Protocol Decision is not warranted.

Finally, FDA has maintained that the best way to accomplish the transition to non-CFC alternative drug products is for each country to develop a national transition strategy that matches the unique characteristics of the regulatory, health care, and marketing environment of the particular country.¹³ FDA recognizes that developing a "one size fits all" international strategy is unacceptable because a strategy devised by one country could cause significant problems if it were "imported" and wholly applied to the U.S. legal and regulatory system.¹⁴ Such is the case here.

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In conclusion, we ask that you notify the U.S. delegation to the Beijing meeting that the U.S. is opposed to the adoption of Decision XI/15.

Respectfully submitted,

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cc: Alfonso Liao Lee, Costa Rica National Ozone Commission
Jane Henney, M.D., Commissioner of U.S. FDA
Madeleine K. Albright, U.S. Secretary of State
Carol M. Browner, Esq., Administrator of U.S. EPA

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- 1 62 Fed. Reg. 10242, 10245 (Mar. 6, 1997).
 - 2 Tamar Nordenberg, *CFC-Free Medication for an Ailing Ozone Layer*, FDA Consumer Magazine (May-June 1997).
 - 3 S. Treaty Doc. No. 10, 100th Cong., 1st Sess., 26 I.L.M. 1541 (Sept. 16, 1987).
 - 4 42 U.S.C. § 7671.
 - 5 64 Fed. Reg. 47719 (Sept. 1, 1999).
 - 6 Statement of Murray M. Lumpkin, M.D., Deputy Director for Review Management, Center for Drug Evaluation and Research, Food and Drug Administration, before the Subcommittee on Health and Environment, Committee on Commerce, U.S. House of Representatives, July 30, 1997 ("1997 FDA Statement by Dr. Lumpkin").
 - 7 1997 FDA Statement by Dr. Lumpkin.
 - 8 1997 FDA Statement by Dr. Lumpkin.

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⁹ FDA's current proposed rule on the use of ozone-depleting substances recharacterizes a violation of the new drug approval process as a "nonessential" use under the Clean Air Act. 64 Fed. Reg. 47719 (Sept. 1, 1999).

¹⁰ FDA proposed slight modifications to these data requirements in 64 Fed. Reg. 47719 (Sept. 1, 1999).

¹¹ See Mead Johnson Pharmaceutical Group v. Bowen, 838 F.2d 1332, 1333 (D.C. Cir. 1988); H.R. Rep. No. 98-857, 98th Cong., 2d Sess., Pt. 1 at 14-15, reprinted in 1984 U.S. Code Cong. & Admin. News 2647-8; 57 Fed. Reg. 17,950-951 (April 28, 1992); Abbott Laboratories v. Young, 920 F.2d 984, 985 (D.C. Cir. 1990), cert. denied, Abbott Laboratories v. Kessler, 502 U.S. 819 (1991).

¹² 21 U.S.C. § 355(j).

¹³ 1997 FDA Statement by Dr. Lumpkin.

¹⁴ 1997 FDA Statement by Dr. Lumpkin.

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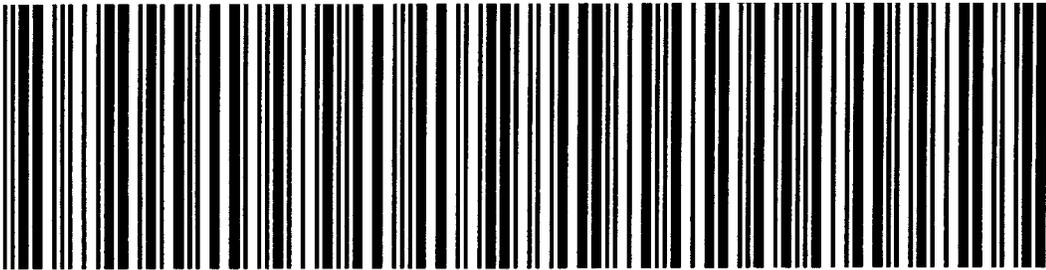
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